



## Neuro Rescue from Nature: Evidence-Based Herbal Strategies for Brain Health

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KEYWORDS	ABSTRACT:
Medicinal Plants, Neurodegenerative Disorders, Molecular Mechanisms, Evidence Based Therapies	Neurodegenerative diseases give a major and growing global health challenge, marked by the continuing decline and decreasing of neurons in specific central nervous system regions. Despite having different clinical characteristics and pathological processes, conditions including Alzheimer's diseases, Parkinson's diseases, Huntington's, and amyotrophic lateral sclerosis share pathways of cellular degeneration and neural abashment . There is an emergency need for novel and disease-modifying approaches due to the increased prevalence of these disorders and the poor efficacy of current therapeutic therapies. Plant-derived phytochemicals have interested a lot of notice recently because of their many neuroprotective qualities, which are backed by centuries of orthodox medicine and increasing scientific confirmation. This manuscript critically examines the journey of phytochemicals from ethnomedical origins to evidence-based therapeutic applications, with a highlight on their methods of action, the results of preclinical and clinical studies, and their possible for use in the management and therapeutic effect of neurodegenerative illnesses.

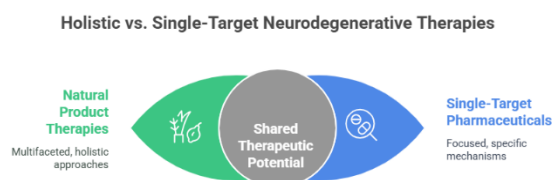
### 1. Introduction

Neurodegenerative diseases, comprise Parkinson's, Alzheimer's disease, Huntington's disease, and amyotrophic lateral sclerosis, are propound by the forward – looking and result oriented degeneration of neurons in specific components of the nervous system. These set-up poses a serious and escalating world health concern (Khan et al., 2020; Sairazi & Sirajudeen, 2020). The complex coordination and regulation execute by the nervous system suit disrupted in these disorders, consecutive series of events weakening effects that significantly impair

everything functioning (Jacquot et al., 2013). Present medical strategies work, focused on symptomatic relief and ease up disease progression, as treatable treatments elusive - emphasise the immediate need for narrative approach targeting the underlying pathological mechanisms (Jacquot et al., 2013; Thapa et al., 2023). The restrictions of existing therapies, along with the arising prevalence of these disorders, operated buoyant research efforts pursue at discovering innovative therapeutic interventions (Kumar & Khanum, 2012).



Medicinal plants, rooted in a rich tradition of bygone use and known for their broad spectrum of bioactive constituents, have emerged as expert personnel seeking for disease-modifying treatments (Pitchai et al., 2019). These natural products provide a comprehensive approach to get to grips with the complex pathogenesis of neurodegenerative diseases, conceivably harmonize multiple molecular pathways simultaneously—undeserving advantage over single-target pharmaceutical agents (Nahar et al., 2025). A revolution with regard to integrative and preventative medicine is constituted by the discovery of phytochemicals for the treatment of neurodegenerative disease, provides hope for improved care result and improved quality of life for (Akkol et al., 2021). The dissimilitude between holistic approaches and single-target therapies in neurodegenerative disease organizing is illustrated in **Figure 1**.



Dopaminergic neurons in the pars compacta of the substantia nigra cautiously deteriorate in Parkinson's, the second most common neurodegenerative disease in the world. Consequently, both motor and non-motor symptoms notably affect life quality (Dubey et al., 2020; Xu et al., 2023). Despite development in traditional therapeutic approaches, effective treatment of Parkinson's disease remains challenging, as it continues to result in substantial disability and mortality (Hosseini-Khannazer et al., 2022).

The most prevalent sort of dementia disorder, Alzheimer's, is exemplified by the accumulation of neurofibrillary tangles (NFTS) and neuritic amyloid plaques in the brain, it causes memory loss and a decline in cognitive function (Stoddard-Bennett & Pera, 2019).

In spite of efforts to develop curative drugs, current neurodegenerative disease treatments mostly focus on symptom management in preference to addressing or backing the disease's progression (Shim et al., 2022; Ntetsika et al., 2021). With per-person expenses estimated between USD 30,000 and USD 60,000 yearly, the financial strain of dementia is enormous, with an estimated USD 800 billion worldwide. It highlights alternative names for economical and effective medical approaches (Martínez-Iglesias et al., 2023).

Potential treatment targets incorporate the complex molecular mechanisms that support these disorders, for instance, neuroinflammation, mitochondrial dysfunction, protein misfolding, and cellular stress. Identifying early therapeutic windows and understanding the first triggers of pathophysiological surge in neurodegenerative conditions like Parkinson's disease and Alzheimer's remain ongoing challenge (Zacharias et al., 2022). The progressive course of these diseases, combined with the world's ageing population, highlights the important need for disease-modifying therapies that can halt or at rearmost slow the degenerative process (Maramai et al., 2020).

The development of in-vivo models that accurately replicate the clinical and pathological functions of neurodegenerative diseases in humans—including amyotrophic lateral sclerosis, Huntington's disease, familial Alzheimer's, and Parkinson's disease—has commenced the pursuit of therapeutics that address disease mechanisms rather than just symptoms. This shift has, to some extent, redirected the field's focus from symptomatic treatment toward potentially transformative, disease-modifying strategies (Golde, 2009).

## 2. Methods

The therapeutic effects of conventional plants and their derived compounds in managing neurodegenerative disorders are a multidimensional area of research require a comprehensive and systematic methodological approach. An exhaustive examination of existing literature is



essential, starting from in vitro experiments to clinical trials (Hao et al., 2018) .

This review combines findings from diverse sources, including Scopus, PubMed, Web of Science, and specialised databases concentrated on traditional medicine and ethnopharmacology (Yang et al., 2024) . The search approach used a merge of keywords related to medicinal plants and central neurological conditions such as Parkinson's disease, Alzheimer's disease, Huntington's disease, and amyotrophic lateral sclerosis, furthermore related molecular processes (Colone et al., 2018) . An obvious evaluation of the full articles in adherence with established criteria for inclusion and exclusion followed an initial investigation of the selected literature using titles and abstracts (Mirgorodskaya et al., 2022). Studies were assessed for methodological rigor, sample size, and robustness of statistical analysis .

Data extraction was restrained by using standardised templates to capture essential information, include plant species, active substances, experimental models, and observed therapeutic outcomes . In vitro studies examining the neuroprotective effects of plant extraction or isolated compounds on neuronal cell lines were examined with particular perception mechanisms such as antioxidant activity, anti-inflammatory responses, and customisation of programmed cell death. In vivo studies using animal models of neurodegenerative diseases—including mutant and lesion-induced models—provided crucial revelations into the efficacy and safety profiles of medicinal plants (Genchi et al., 2024) .

Clinical investigations on the impact of herbal therapies on central nervous system function, interoperability, and the quality of life in patients with neurodegenerative disorders were critically examined . Systematic reviews and meta-analyses offered a quantitative synthesis of present proof, providing justifiable estimations of the therapeutic effect sizes of medicinal plants. Both preclinical and clinical data were conscientiously examined to identify promising candidates for further investigation (Nahar et al., 2025) . Ultimately, a

comprehensive approach- combining across different stages of research was necessary to completely understand the medicinal properties of plant-derived medicines (Akkol et al., 2021).

The rectitude of ethnobotanical knowledge with modern scientific methods represents a confirm key step in the traditional use of therapeutic plants (Karunamoorthi et al., 2012). Ethnobotanical fieldwork and discussion with traditional shaman offered valuable perspectives on the selection of plant species historically employed in treating neurological ailments (Karunamoorthi et al., 2012).

Identifications of bioactive ingredients from old medicinal plants was typically achieved through a mixture of extraction, isolation, and purification techniques, often guided by bioassay-directed fractionation. The observed therapeutic outcomes were frequently ascribed to synergistic interactions among many phytochemicals present in whole plant extraction (Sharifi-Rad et al., 2020).

Moreover, the pharmacological usage of medicinal plants align with traditional medicine's comprehensive approaches, which emphasise multitarget strategies using complex formulations (Kosanam & Pasupula, 2021; Wang et al., 2025). Studying potential synergistic interactions among these compounds was essential for fully illuminate the therapeutic efficacies of plant extracts (McClatchey et al., 2009). The application of plant-based natural medicine also present a hopeful path for alternative therapies in the treatment of psychiatric diseases and neurological conditions (Remali & Aizat, 2024).

Advanced analytical techniques such as Liquid Chromatography–Mass Spectrometry (LC–MS) and Nuclear Magnetic Resonance (NMR) Spectroscopy were employed to detect and quantify the chemical constituents of medicinal plants. The mixture of different data sources was essential for developing a holistic view of the neurotherapeutic potential of these botanical resources. A mechanistic overview of plant-derived nano formulations in neurotherapeutics is presented in **Table 1**.



Table 1. Mechanistic Overview of Plant-Derived Nanoformulations in Neurotherapeutics

Therapeutic Approach	Phytochemical / Drug Used	Target Disease	Formulation Type	Mechanism of Action	References
Use of lipid-based nanocarriers	Bioactive compounds (e.g., curcumin, antipsychotics)	Neurological diseases, cancer	Solid lipid nanoparticles, liposomes	Improved bioavailability & Blood-Brain Barrier (BBB) penetration	Dhiman et al., 2021; Ferreira et al., 2023; Furtado et al., 2018
Use of natural antioxidants	Curcumin	Neurodegenerative diseases (e.g., Alzheimer's)	Oral bioavailable formulations, nanoparticles	Neuroprotectant via anti-inflammation effect and antioxidant effects	Genchi et al., 2024
Anti-inflammatory therapy	<i>Ganoderma lucidum</i> extract	Neuroinflammation	Crude extract or encapsulated form	Inhibition of MAPK & NF- $\kappa$ B pathways	Hilliard et al., 2020
Neuroprotection using flavonoids	Hesperetin (Citrus flavonoid)	Neurological Disorders	Nutraceutical/Oral Supplement	Antioxidant and anti-inflammatory effects via NF- $\kappa$ B and cytokine modulation	Khan et al., 2020
Neuroinflammation control	Glucocalyxin-A	Neuroinflammation	Plant Extract	Inhibits p38 MAPK & NF- $\kappa$ B signaling pathways	Kim et al., 2013
Neuroprotection	Saururus chinensis extract	Neurotoxicity / Neuroinflammation	Crude Plant Extract	Modulation of NF- $\kappa$ B pathway and oxidative stress	Kim et al., 2014
Wound healing and antioxidant therapy	Abietic Acid	Wounds, Oxidative Stress	Microemulsions and Emulgels	Antioxidant activity and enhanced tissue regeneration	Mirgorodskaya et al., 2022
Anti-Parkinsonian	Schisantherin A	Parkinson's Disease	Natural compound formulation	Optimized pharmacokinetics; neuroprotective action	Sa et al., 2015



### 3. “Therapeutic Potential of Medicinal Plants in Neurodegenerative Disorders”

Medicinal plants here probable in drug discovery, particularly for neurodegenerative disorders (Fabricant & Farnsworth, 2001). Traditional medicine systems hold a wealth of experience knowledge concerning plant species with medicinal properties. Approximately 80% of the human population depends on phytomedicine as their initial source of healthcare, underscoring their cultural and medical relevance (Bourhia et al., 2020; WHO, 2008).

Multiple modern pharmaceuticals are derived from or inspired by bioactive plant compounds (Ssenku et al., 2022). Advancements in technologies have sped up the screening and recognition of active compounds in natural products (Buenz et al., 2017; Newman & Cragg, 2016). Detailed studies on plant-derived substances have helped the development of many conventional medicines (Caballero-Gallardo et al., 2025; Cragg & Newman, 2013). The wide chemical diversity of phytochemicals offers new answers to complex medical problems (Chaachouay & Zidane, 2024; Swarnkar et al., 2019). Nature-based therapies have been make use of for hundreds of year by traditional medicinal systems such Traditional Korean Medicine, Unani, and Traditional Chinese Medicine (TCM) Kampo (Bhardwaj et al., 2021; Efferth et al., 2020).

#### 3.1 Therapeutic Applications

Plants produces a wide range of secondary metabolites with diverse biological functions, positioning them as a rich source of therapeutic candidates (Mahapatra et al., 2021). Despite the rise of synthetic pharmaceuticals, plants remains central to healthcare, particularly in low-resource mounting (Sharma et al., 2021; Fabricant & Farnsworth, 2001).

Worldwide, over 25% of prescription medications are derived from plants (Alafnan et al., 2021; Newman & Cragg, 2020). The FAO estimates that 50,000 plant

varieties are used in traditional medicine globally (Bukke et al., 2011; WHO, 2019). The high, accessibility, and cultural acceptability of plants are what motivate their use in medicine (Zakaria et al., 2020; Pieme et al., 2014; Fabricant & Farnsworth, 2001). Diterpenoids, terpenoids, alkaloids, and flavonoids are examples of active ingredients with pharmacological potential (Bona et al., 2020; Hussain et al., 2012; Kinghorn, 1994; Zhang et al., 2013; Cragg et al., 2011).

Comprehension that the cooperative action between compounds in full plant extracts is essential for maximising medicinal efficacy (Elshamy et al., 2019; Wagner & Ulrich-Merzenich, 2009). Spices used in cooking have also revealed medicinal properties (Mahapatra et al., 2021; Srinivasan, 2014). Multicultures, traditional plant remedies are deeply rooted in spiritual and social practices (Rodríguez-Negrete et al., 2024).

#### 3.2 Anti-Apoptotic Pathways

Medicinal plants excluding into multiple processes, including modulation of neurotransmission, antioxidant activity, anti-inflammation actions, and neuroprotection. Secondary metabolites like alkaloids, terpenoids, and polyphenols have shown broad pharmacological activity (Chakrabarty et al., 2022; Dash et al., 2021; Dekebo, 2019; Kumar et al., 2016).

Particular phytochemicals enhance the activities of endogenous antioxidant enzymes—such as Superoxide Dismutase enzyme and Glutathione Peroxidase enzyme – by that means protecting neurons from oxidation stress (Dash et al., 2021; Jamloki et al., 2022; Mohsenipour & Hassanshahian, 2015; Ramírez-Gómez et al., 2019; Liu et al., 2017). These metabolic binding with molecular regions in the brain, including receptors, enzymes, and signaling pathways, to consult neuroprotection. This renascent in plant-based healthcare is driven by growing concerns over drug hostility and side effects related with synthetic drugs (Hikisz & Bernasińska, 2021; Zhakipbekov et al., 2024; Cragg & Newman, 2013).



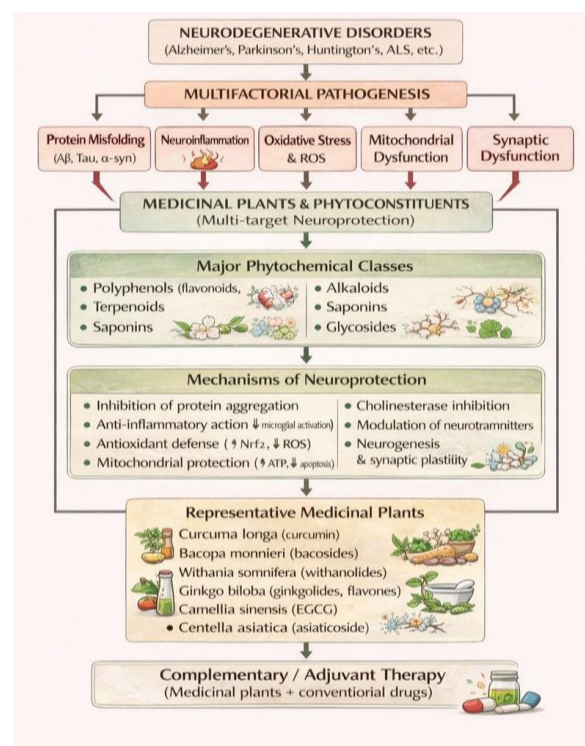
Phytochemical	Plant Source	Neurodegenerative Disease(s)	Mechanism of Action	Clinical Use	Reference
Nectandra angustifolia extract	<i>Nectandra angustifolia</i> (Laurel Amarillo)	Neuroinflammation-related disorders	Anti-neuroinflammatory via reduction in pro-inflammatory cytokines	Preclinical evidence for neuroinflammation modulation	Crescitelli et al., 2023
MSC-secreted antioxidant factors	Not plant-based (Mesenchymal Stem Cells)	Oxidative stress-related neurodegeneration	Antioxidant, anti-apoptotic, neuroprotective	Investigated in regenerative therapies	Angeloni et al., 2020
Phytochemicals in <i>Annona muricata</i>	<i>Annona muricata</i>	Potential CNS application (preclinical)	Antiproliferative, induces apoptosis, antioxidant	Investigational neurotherapeutics	Pieme et al., 2014;

Medicinal plants therapeutic information is given in **Table 2**.

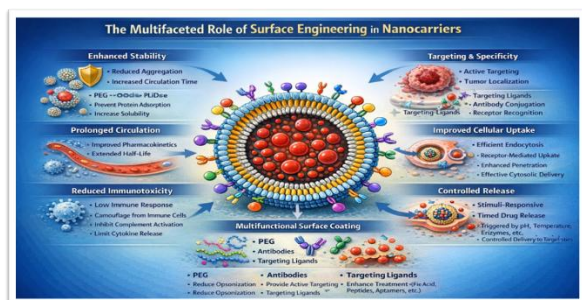
### 3.3 Nanotechnology-Mediated Delivery of Phytoconstituents for CNS Disorders

Nanoparticles (NPs) offer a auspicious for overcoming blood–brain barrier (BBB) limitations in treating neurodegenerative disorders (Zhao et al., 2020; Zhu et al., 2021; Saraiva et al., 2016). Engineered nanomaterials—organic, inorganic, or carbon-based—can be administered via oral, nasal, dermal, or respiratory routes (Zhu et al., 2021).

NPs increases site-specific targeting, modulate inflammatory responses, and extend drug distribution by avoiding degradation (Onoue et al., 2014; Singh & Lillard, 2009; Nance et al., 2014). However, challenges such as improvement by the reticuloendothelial system (RES) and poor penetration remain (Vega-Baudrit, 2019). Lipid-based systems, dendrimers, micelles, nanoemulsions, and polymeric NPs have shown word of honour in CNS delivery (Sultana et al., 2020; Sezer, 2014; Kakkar & Kaur, 2011). While reducing systemic adverse effects, the increased permeability and retention impact promotes NP accumulation at sick locations (He et al., 2023; Grebler et al., 2025). Figure 2 shows based nanoformulations in neurodegeneration.



**Figure 2. Potentiality of medicinal plants in neurodegenerative disorders**



**Figure 3. Multifaceted impact of nanoparticle surface modification**

### 3.4 Surface Modifications and Functionalization Strategies

Surface modification of NPs is pivotal for upgrade drug delivery, targeting, and immune evasion (Siafaka et al., 2016; Tiwari et al., 2019). Techniques such as

PEGylation extend circulations time and decrease RES clearances (Dhiman et al., 2021; Dadwal et al., 2018). Ligands like aptamers, peptides, and antibodies can be fond of to enhance specificity and drug accumulation (Su & Kang, 2020; Xu et al., 2022; Bertrand et al., 2014).

Advanced softening include the use of thiomers, CD47 mimics, and stimuli-responsive coatings for pH, temperature, or enzyme-triggered drug release (Mendes et al., 2022; Choi et al., 2009; Firouzabadi et al., 2022; Yan & Ding, 2020; Blanco et al., 2015). The multifaceted role of surface engineering in nanocarriers is detailed in **Figure 3**.

### 3.5 Oxidative Stress and Antioxidant Defence

Oxidative damage, resulting from excess reactive oxygen species (ROS), is a determining factor in neurodegenerative pathogenesis (Gao et al., 2025; Uttara et al., 2009). ROS fails lipids, DNA, and cellular proteins, leading to neuronal death

Medicinal plants are high in antioxidants like polyphenols, flavonoids, and alkaloids that neutralise

ROS and inhibit lipid peroxidation (Schneider, 1998; Peña-Bautista et al., 2019; Halliwell & Gutteridge, 2015). These compounds also increases neuroplasticity and cognitive function (Parasram, 2017; Vauzour et al., 2010). The Nrf2 signaling pathway is a urge maintainces of antioxidant responses in the CNS (McBean et al., 2016; Carvalho et al., 2016; Bellezza et al., 2018).

Present research indicates that mesenchymal stem cells (MSCs) or their secretomes may decrease inflammation, enhance neurotrophins, and increase antioxidant capacity (Angeloni et al., 2020; Chen et al., 2016). Disturbances in membrane asymmetry and nuclear integrity further contribute to vascular dysfunction and neuroinflammation (Chong et al., 2005).

High antioxidant intake from plants correlates with a decreased risk of neurological diseases, though therapeutic efficacy is affected by dosage, timing, and disease development (Carvalho et al., 2018; Cichoń et al., 2021; Liu et al., 2017; Spencer, 2010).

### Neuroinflammation and Anti-Inflammatory Potential of Medicinal Plants

Neuroinflammation is a big contributor to neuronal death in disorders like Parkinson's & Alzheimer's disease. It is driven by microglial and astrocytic activation, and the accumulation of cytokines such as iNOS, TNF- $\alpha$ , IL-1 $\beta$ , IL-6, and COX-2 (Kim et al., 2014; Perry et al., 2010). Targeted modulation of these mediators offers therapeutic benefit (Qiburi et al., 2021).

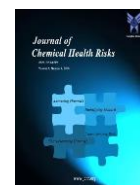
Phytochemicals in medicinal plants lessen inflammatory cytokines and decrease microglial activation (Crescitelli et al., 2023; Rahman et al., 2021). "TCM plants such as *Andrographis paniculata*, and biochemicals like flavonoids, indoles, and tetramethylpyrazine, have demonstrated potent anti-inflammation effect and neuroprotection (Xu et al., 2016; Sa et al., 2015; Kumar & Khanum, 2012; Singh & Kakkar, 2020).

"Edible and medicinal mushrooms are also attracting for their anti-inflammatory potential (Hilliard et al., 2020; Wasser, 2017). "Interventions that target early microglial activation show promise for hesitant the progression of chronic neuroinflammation (Kim et al., 2013; Zhu et al., 2021).

Clinically approved phytochemicals with neuroprotective effects are summarized in **Table 3**

### 4. Challenges, Future Prospects and Conclusions

Neurodegenerative disorders characterize a worsening global health difficulty due to their complex, improving nature and restricted curative treatment. Because neurodegenerative diseases are complicated, progressing, and have few medical therapies, they constitute a growing threat to world health. The



requirement for disease-modifying techniques that go beyond symptomatic upgrading is emphasised by the author. therapeutic plants. They are a viable option for addressing several disease pathways concurrently due to their great phytochemical variety and venerable background of use in medicine . The effectiveness of these plant-based chemicals is greatly increased by developments in nanotechnology-driven delivery methods. The integration of ethnobotanical understanding with new techniques and scientific methods could surface the way for more holistic, safe,

and reachable treatments for neurodegenerative diseases . Traditional medicines and herbs have become incorporated into modern medicine . These traditional medicines are motionless used today by a bulk majority of the population .

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Phytochemical	Plant Source	Neurodegenerative Disease(s)	Mechanism of Action	Clinical Use	Reference
Flavonoids, terpenoids, etc.	Lamiaceae family plants	Cardiovascular comorbid neurodegenerative diseases	Antioxidant and anti-inflammatory properties	Used in functional foods and traditional medicine	Chakrabartty et al., 2022
Kaempferol, essential oils	Kaempferia species	Neuroinflammation, oxidative stress	Antioxidant, anti-inflammatory, neuroprotective	Explored in traditional medicine, preclinical	Elshamy et al., 2019
Citral, flavonoids	Cymbopogon citratus (Lemongrass)	Oxidative stress-related neurodegeneration	Antioxidant, cytoprotective	Folk medicine use; in vitro data	Erhabor et al., 2019
Isoliquiritigenin	Licorice root (Glycyrrhiza species)	Alzheimer's disease	Targets inflammation, apoptosis, and Aβ metabolism	Preclinical validation (in vitro & in vivo)	Gao et al., 2025
Curcumin	Curcuma longa (Turmeric)	Alzheimer's, Parkinson's, Huntington's diseases	Antioxidant, anti-inflammation, anti-amyloid, neurogenesis	Dietary supplement; in clinical trials	Genchi et al., 2024
Ganoderic acids, polysaccharides	Ganoderma lucidum (Reishi mushroom)	General neuroinflammation	Inhibits NF-κB and MAPK in microglia	Traditional use; anti-inflammatory supplement	Hilliard et al., 2020
Bromelain	Ananas comosus (Pineapple)	Indirect link (anti-inflammatory relevance)	Reduces cytokines and oxidative stress	Nutraceutical use	Hikisz & Bernasińska, 2021
Hesperetin	Citrus spp. (e.g., oranges)	Alzheimer's, Parkinson's, Huntington's	Antioxidant, anti-inflammatory; inhibits ROS production, modulates MAPK/NF-κB signaling	Neuroprotection, cognitive enhancement	Khan et al., 2020;
Glucocalyxin-A	Rabdosia japonica	Alzheimer's, neuroinflammation	Inhibits NF-κB and p38 MAPK signaling in microglia; reduces neuroinflammation	Anti-neuroinflammatory agent	Kim et al., 2013;



Quercetin Various flavonoids	Saururus chinensis	Alzheimer's, Parkinson's	Inhibits NF- $\kappa$ B, antioxidant activity, reduces LPS-induced neurotoxicity in microglial cells	Herbal anti- inflammatory neuroprotective therapy	Kim et al., 2014;
Schisantherin A	Schisandra chinensis	Parkinson's	Antioxidant and dopaminergic neuroprotection, enhanced bioavailability via nanodelivery	Anti-parkinsonian therapy	Sa et al., 2015;
Flavonoids, polyphenols	Aegle marmelos	Alzheimer's (potential), CNS disorders	Antioxidant, anti- inflammatory	Used in traditional CNS tonic formulations	Swarnkar et al., 2019;
Andrographolide	Andrographis paniculata	Peripheral neurodegeneration; potential PD	Anti- inflammatory, promotes Schwann cell proliferation and neurotrophic factors (BDNF, GDNF, CNTF); supports nerve regeneration	Potential in peripheral nerve injury recovery; neuroregeneration	Xu et al., 2016

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